



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

“We are now rolling out vaccination to high-risk groups and this is going to provide a very strong selection pressure,” says Emma Thomson at the University of Glasgow. “We may well see a rapid rise in mutations as a result.”

We will also have to keep an eye out for viruses that can evade natural immunity, she says. Virologists have already discovered variants that are able to partially evade antibodies.

These are a wake-up call. Even though the UK variant, known as B.1.1.7, doesn’t seem to have an escape mutation, the fact that its spike protein is 17 mutations away from the original is “a little bit

terrifying”, says Robertson.

“It is a concern that a large number of spike mutations are found in the same strain,” says Kumar.

One potential danger that we can probably stop worrying about is recombination, which occurs when two related coronaviruses mash their genomes together to create a hybrid. Two studies scouring thousands of viral genomes have found no evidence that this has occurred.

But escape mutation is a real and present danger. A recent case study highlights what could happen once we put the virus under heavy selection

pressure. In May 2020, an immunocompromised patient was admitted to a UK hospital with covid-19. He died of the disease in August. Over the 101-day course of his illness, a team led by Ravindra Gupta at the University of Cambridge repeatedly sampled and sequenced viruses from the patient’s respiratory tract.

The virus strikes back

The patient was given infusions of an antiviral therapy called convalescent plasma – an antibody-rich blood extract from another person infected with the virus.

Days later, Gupta’s team saw a dramatic rise in a mutant version of the coronavirus and later confirmed that it had partially escaped the therapeutic effects of the plasma. This mutant virus eventually killed the patient.

We mustn’t draw too many conclusions from this single case, says Gupta. The patient was also being treated for cancer and couldn’t mount an effective immune response of his own. But the study shows how quickly and viciously the virus can mutate and escape under selection pressure.

The answer to these threats is surveillance, to flag up and isolate escape mutants before they spiral out of control. The UK’s world-class surveillance system relies on a combination of monitoring and sequencing. Red flags are raised if something unusual happens clinically or epidemiologically, and then geneticists search for mutant viruses that could be responsible.

The new UK variant, for example, was spotted because lockdown restrictions were reducing viral spread everywhere but Kent. Surveillance would also

What are the new coronavirus variants?

THERE are tens of thousands of variants of the SARS-CoV-2 virus that differ from each other by at least one mutation, according to sequencing studies that track its spread and monitor how it is evolving.

Many of these variants die out, but others spread and acquire further mutations. Overall, though, the coronavirus hasn’t changed much. Any two SARS-CoV-2 coronaviruses from anywhere in the world will usually differ by fewer than 30 mutations, and they are all still regarded as one strain.

In early December, scientists looking for reasons for a rapid growth of case numbers in Kent in south-east England, noticed that one variant, now known as B.1.1.7, was spreading faster than others. The evidence that it is more transmissible is growing ever stronger.

This variant is spreading faster than different variants in other regions of the UK and in at least three other countries: Ireland,

Denmark and Switzerland. It has reached many other countries, too, but because most countries sequence far fewer samples than the UK or Denmark do, it isn’t yet clear whether it is outcompeting other variants in these countries as well.

Initial studies suggest that B.1.1.7 is about 50 per cent more transmissible than other variants. This might not sound like much, but it makes a huge difference over time.

Another new variant, known as B.1.351, was discovered in South Africa after an unusual surge in coronavirus cases beginning in October. It is thought to spread faster too, but there is less evidence than for B.1.1.7.

Why these variants spread faster is unclear (see page 11). B.1.1.7 has 17 defining mutations, and B.1.351 has nine. The overall number of mutations isn’t unusual and many of them have been found before.

There has been much focus on the only mutation common

to both viruses, known as N501Y. However, this was first seen last April, in Brazil, and a variant with it circulated in Wales for a while, so this alone cannot explain the higher transmissibility.

With many countries now looking for the new variants, reports are emerging of other versions with similar changes. In particular, the P.1 variant found in Brazil has nearly the same three mutations in the spike protein as B.1.351.

Reports of two new variants have also emerged in the US, one of which also has the N501Y mutation, as well as another mutation seen on B.1.1.7. However, it remains unclear if any of these other variants also spread faster.

B.1.1.7 and its ilk will continue to change, so there is a risk they could become even more dangerous. The more people they infect, the more chances there are for these viruses to evolve further.

Michael Le Page

“Even though this virus is evolving slowly, we have to take surveillance very, very seriously”

be triggered if vaccinated people or those who had recovered started falling ill, says Kumar.

About 10,000 genomes a week are sequenced in the UK and there are plans to up that to 20,000 by March. The country also has a new body called the G2P-UK National Virology Consortium to keep track of new mutations and warn about potentially dangerous ones.

“Even though this virus is evolving slowly, we do really have to take surveillance very, very seriously,” says Robertson. ■